56. (New) The expression vector of claim 53, wherein at least one of said silencer elements is a neuron restrictive silencer (NRS) element to which neuron restrictive silencer (NRS) transcription factor binds.

57. (New) The expression vector of claim 53, wherein at least one of said silencer elements is a negative regulatory element (NRE) or repressor.

B8 cont'd

58. (New) The expression vector of claim 53, wherein at least one of said conditionally inducible elements is a hypoxia response enhancer (HRE) element to which hypoxia inducible factor-1 (HIF-1) transcription factor binds.

59. (New) The expression vector of claim 53, wherein at least one of said conditionally inducible elements is an NF-κB responsive element to which NF-κB transcription factor binds.

REMARKS

The specification has been amended at page 10, lines 16-29, to incorporate the language and disclosure of originally filed claims 13 and 16. A marked version showing the amendments to the specification is attached hereto as Exhibit A. This amendment is supported by originally filed claims 11, 13 and 16, and in the specification at page 36, lines 17-24. The above-made amendments contain no new matter. *See* Exhibit A.

Claims 1-41 are pending in the application. Claim 30 has been canceled, and claims 28-29 and 31-41 have been canceled as drawn to non-elected subject matter, without prejudice to Applicants' right to prosecute these claims in related applications. In the instant amendment, claims 1, 3, 4, 6, 7, 11, 13 and 16-23 have been amended to clarify the present invention. New claims 42-59 have been added. Upon entry of the above-made amendment, claims 1-27 and 42-59 will be pending. A marked version of the amended claims showing changes made is attached hereto as Exhibit B. A clean version of the pending claims, as amended, is attached hereto as Exhibit C.

Support for the amended claim recitations and for the new claims may be found in the specification as follows:

Claim	Support in specification
1	Page 3, lines 19-22; page 3, line 26 to page 4, line 5

3	Page 11, lines 15-18
4	Page 11, lines 15-18; page 21, line 31 to page 22, line 8
6	Page 11, lines 15-18, 23-25; page 21, line 31 to page 23, line 8
7	Page 10, lines 11-12; page 21, lines 31-32
11	Example 3; FIG. 3
13	Original claim 13
16	Original claim 16; page 12, lines 1-11
17	Example 3
18	Page 13, lines 30 to page 15, line 9
19	Page 13, lines 2-9
20	Page 14, lines 2-5; page 17, lines 16-22; page 20, lines 22-26; page26, lines 25-31
21	Page 6, lines 10-11
22	Page 8, lines 8-12
23	Page 19, lines 7-10
42	Page 9, lines 13-18
43	Page 8, lines 8-10
44	Page 8, lines 8-11
45	Page 8, lines 8-11
46	Page 6, line 32 to page 7, line 3
47	Page 6, line 32 to page 7, line 3
48	Example 1
49	Example 1
50	Example 1; FIG. 2
51	Example 1
52	Example 1
53	Page 6, lines 7-10; page 9, lines 32-33
54	Page 11, line 16; Example 1
55	Page 11, lines 15-18
56	Page 10, lines 11-12; page 30, lines 31-32
57	Page 10, lines 3-15; Example 1
58	Example 1
59	Example 3

No new matter has been added by the amendments to claims 1, 3, 4, 6, 7, 11, 13 and 16-23, or by new claims 42-59. Entry of the foregoing amendments is respectfully requested.

CONCLUSION

Applicants respectfully request entry of the foregoing amendment and remarks into the file of the above-identified application.

Respectfully submitted,

By: Lawrence S. Graham Reg. No. 49,020

Adriane M. Antler 32,605

Date November 6, 2002

Adriane M. Antler (Reg. No.)
PENNIE & EDMONDS LLP
1155 Avenue of the Americas
New York, New York 10036 2711
(212) 790-9090

Enclosures

EXHIBIT A: MARKED VERSION SHOWING CHANGES MADE IN THE SPECIFICATION
U.S. PATENT APPLICATION SERIAL NO. 09/723,326
(ATTORNEY DOCKET NO. 10989-004-999)

(As amended November 6, 2002)

Please replace the paragraph at page 10, lines 16-29 with the following paragraph:

A "conditionally inducible element" is an element of the expression vector that confers positive regulation on transcription of a downstream expressed region under inducing conditions. It may be obtained from enhancer regions that are also conditionally inducible, but constitutively active enhancers that increase basal transcription under most or all conditions [is] are not [a] preferred [source] sources for conditionally inducible elements. Removal of a conditionally inducible element from an expression vector would be expected to decrease expression of a downstream region under inducing conditions. As described above, it may be present at least one, two, three, four, five, six or more times as a homomultimer (i.e., repeats of the same conditionally inducible element) or a heteromultimer (i.e. a mixture of different conditionally inducible elements or variations thereof). Conditionally inducible elements (e.g., consensus sequences known in the art) are usually between about 4 and 100 nucleotides in length. The conditionally inducible element may or may not be active in most cells, but under non-inducing conditions, the latter situation is preferred. Examples of conditionally inducible elements include the hypoxia response enhancer (HRE) element, to which hypoxia inducible factor-1 (HIF-1) binds; HRE elements to which HIF-1α does not bind, for example, the metallothionein I (MT-I) and metallothionein II (MT-II) elements bound by metallothionein transcription factor-1 (MTF-1); metal response elements; heat response elements; hormone response elements; NF-κB response elements; and growth factor response elements.

EXHIBIT B: MARKED VERSION OF AMENDED CLAIMS
U.S. PATENT APPLICATION SERIAL NO. 09/723,326
(ATTORNEY DOCKET NO. 10989 004-999)

(As amended November 6, 2002)

1. (Amended) An isolated expression vector comprised of (a) one or more silencer elements and one or more conditionally inducible elements to form a silencer-inducible region, and (b) a promoter in operative linkage with at least one silencer-inducible region, wherein said promoter is thereby regulated by said at least one silencer-inducible region, and said promoter is upstream of at least one nucleotide sequence [expressed region]; said expression vector under an inducing condition expressing said at least one nucleotide sequence [downstream region] in an amount greater than expression of said at least one nucleotide sequence [downstream region] without said inducing condition.

3. (Amended) The expression vector of claim 1, wherein said promoter is a mammalian promoter active in a plurality of [several] different tissues.

4. (Amended) The expression vector of claim 3, wherein said mammalian promoter is active in one or more [different] tissues selected from the group consisting of cardiac muscle skeletal muscle, vascular endothelium, brain, retina, kidney, liver, lung, bone marrow and spleen.

6. (Amended) The expression vector of claim 5, wherein said cell-type specific promoter is selected from the group consisting of a cardiac muscle-specific [promoters] promoter, a skeletal muscle-specific [promoters] promoter, an endothelial cell-specific [promoters], a neuron-specific [promoters] promoter, a glia-specific [promoters] promoter, a retina-specific [promoters] promoter, a kidney-specific [promoters] promoter, a liver-specific [promoters] promoter, a lung-specific [promoters] promoter, a lymphocyte-specific [promoters] promoter, a mycloid-specific [promoters] promoter, and a tumor-specific [promoters] promoter.

7. (Amended) The expression vector of claim 1, wherein at least one of said silencer elements is a neuron restrictive silencer (NRS) element to which [bound by] neuron restrictive silencer (NRS) transcription factor binds.

11. (Amended) The xpression vector of claim 1, wherein at least one of said conditionally inducible elements is a hypoxia response enhancer (HRE) element to which [bound by] hypoxia inducible factor-1 (HIF-1) transcription factor binds.

13. (Amended) The expression vector of claim [11] 1, wherein HIF-1 does not bind said HRE element [is not bound by HIF-1a including for example metallothionein I (MT-I) and metallothionein II (MT II) bound by metallothionein transcription factor-1 (MTF-1)].

16. (Amended) The expression vector of claim 1, wherein at least one of said conditionally inducible elements is selected from the group consisting of a metal response [elements] element (MRE), a heat response [elements] element, a hormone response [elements] element, and a growth factor response [elements] element.

17. (Amended) The expression vector of claim 1, wherein at least one of said conditionally inducible elements is an N F-κB responsive element to which [bound by] NE-κB transcription factor binds.

18. (Amended) The expression vector of claim 1, wherein said at least one nucleotide sequence [expressed region] is [selected from the group consisting of] a functional coding region [regions] of a gene selected from the group consisting of [genes designated] adenosine deaminase, angiopoietins, apoptosis inhibitor protein [proteins], angiostatin, B-cell CLL/lymphoma (BCL2), catalase, deoxyribonuclease, DT-diaphorase, endostatin, erythropoeitin, fibroblast growth factors (FGF), fumagillin, 13-globin, glutathione peroxidase, granulocyte-colony stimulating factor (G-CSF), granulocyte macrophagecolony stimulating factor (GM-CSF), heat shock transcription factor, hepatocyte growth factor (HGF), interferons, tissue metalloproteinase inhibitor [inhibitors], nitric oxide synthases, platelet derived growth factor [factors] (PDGF), proliferin, somatomedin C (IGF-1), superoxide dismutase, survivin, thymidine kinase, tissue plasminogen activator, tumor protein p53 (TP53), urokinase, and vascular endothelial growth factors (VEGF).

19. (Amended) The expression vector of claim 1, wherein said at least one nucleotide sequence [expressed region] is [selected from the group consisting of] a functional

coding region [regions] of a reporter gene [genes] selected from the group consisting of [designated] chloramphenicol transferase, green fluorescent protein [proteins], red fluorescent protein, β--galactosidase, β-glucoronidase, β-lactamase, and luciferase [luciferases].

20. (Amended) The expression vector of claim 1, wherein said at least one nucleotide sequence [expressed region] is [selected from the group consisting of] a functional portion [portions] of a gene [genes] selected from the group consisting of [designated] MDM2, tumor protein p53 (TP53), endothelin-1, tumor necrosis factor (TNF) [factors (TNFs)], interleukin [interleukins], interferon (IFN) [interferons (IFNs)], vascular endothelial growth factor (VEGF) [factors (VEGFs)], and other cytokines, and wherein said expressed region is positioned in the antisense orientation relative to said promoter.

21. (Amended) The expression vector of claim 1, wherein at least one silencer element and at least one conditionally inducible element are heterologous with respect to each other [in said silencer-inducible region]

22. (Amended) The expression vector of claim 1, wherein at least one silencer element and one conditionally inducible element are arranged within 500 nucleotides of each other [in said silencer-inducible region].

23. (Amended) The expression vector of claim 1 which is a plasmid present in a formulation [formulated] for introduction into a cell by a technique selected from the group consisting of electroporation, [naked DNA delivery,] microinjection, and infusion.